amendment filed on June 30, 2000, but the rejection over Horstmann *et al.* had been previously withdrawn, and its reinstatement could not possibly have anything whatsoever to do with any amendments on applicants' part. It is therefore respectfully requested that the finality of this rejection be withdrawn.

It is also requested that the Examiner consider the following remarks, and on the basis of same now withdraw the rejections herein, including that over Horstmann *et al.* Turning first to the Examiner's position under § 112, claims 84 and 85 have been rejected under that statute as containing subject matter not described in the specification as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. The Examiner thus contends that the applicants now claim "hydrophobic" polymers, but provide no support for that term. The Examiner contends that the polymers on page 15, lines 11-24 which applicants assert are hydrophobic include polymers which are hydrophobic, hydrophilic, and water-soluble. This rejection is respectfully traversed for the reasons set forth hereinafter.

Turning to the specification, the overall thrust of that specification includes one aspect, indeed the most preferred aspect thereof, in which transdermal formulations including highly plasticizing drugs in free-base form are utilized. It is this preferred embodiment of the present invention which is highlighted throughout that specification. The Examiner, however, has referred to the somewhat broader disclosure at page 15 of the specification to support the position that the

specification does not support the use of hydrophobic adhesives. That portion of the specification, however, specifically states that "[w]hile...the adhesive formulations useful with highly plasticizing drugs are defined more restrictively, the adhesive formulation useful in accordance with the present invention may include any adhesive useful in accordance with the creation of transdermal patches." This portion of the disclosure then goes on to list a number of adhesives, most of which are hydrophobic, but some of which are not quite so hydrophobic, as stated by the Examiner. However, beginning at the top of page 18, applicants then go on to specify that, when these patches of the present invention are to be used to deliver highly plasticizing drugs, a more specific group of acrylic-based adhesives has been found to be useful. The disclosure then specifies the adhesives to be so used, and it is clear beyond question that these are the hydrophobic adhesives which are the subject of amended claim 84. Indeed, the overall discussion of the plasticizing effect of these drugs, the need to keep other plasticizing compounds out of the formulation, and the express requirement for employing only non-aqueous solvent systems throughout, makes it clear that neither the presence of water, nor the use of hydrophilic adhesives which would draw water into the system, would be within the scope of their invention. Indeed, at the bottom of page 34, applicants set forth the reasons why non-aqueous solvents must be used in accordance with their invention. One of ordinary skill in the art would certainly not even suggest going beyond the types of hydrophobic adhesives which are specified throughout the specification for use in connection with these highly

plasticizing drugs. It is therefore again respectfully submitted that the specification clearly does disclose and, in fact, specify, at least to one of ordinary skill in this art, the hydrophobic acrylic adhesives and the like which are required for use with these highly plasticizing drugs.

Beyond that, this rejection has also been made with respect to claim 85. Claim 85 is specifically limited to acrylic-based adhesives, and there is, of course, no question as to the support for this limitation in the specification. It is therefore respectfully requested that the objection to these claims under § 112 be withdrawn.

Claims 84 and 85 have been rejected as being unpatentable over Horstmann *et al.* under 35 U.S.C. § 102(b). The Examiner contends that Horstmann *et al.* teaches a transdermal patch comprising islands containing an active in which the islands are obtained by stray drying solutions of active on a moisture-absorbing basic material. Scopolamine liquid is said to be specified and polymers such as polyisobutylene and polyacrylic esters are disclosed. In response to applicants' argument that the now-claimed hydrophobic polymers differ from Horstmann *et al.*, the Examiner notes that applicants also disclosure polyisobutylene and polyacrylic esters at page 15, line 16 to page 16, lines 3-9 of the specification. This rejection is respectfully traversed in view of the above arguments and for the reasons set forth hereinafter.

The Hortsmann *et al.* patent relates to a transdermal therapeutic system having a layered structure including a matrix

layer including a reactive substance, which is activatable, applied to a backing layer, and a separate layer controlling the access of cutaneous liquid. In discussing the efficacy of transdermal applications, as well as the problems associated with same in the background section of this patent, the patentees discuss their object of providing a transdermal therapeutic system which exhibits increased active substance flow and which is stable in storage. This was said to be accomplished by the layered structure of this patent, which includes a matrix 12 (see FIG. 1) containing the active substance and being activatable, as well as a layer 13 controlling the access of cutaneous liquid. Thus, the matrix itself consists of a basic material 15 which is permeable to water vapor, but substantially water insoluble and mainly free of active substance. The basic material comprises islands 14 which are distributed therein, and which consist of a solid pharmaceutical solution and a basic material which is water soluble or water swellable, and in which the matrix is activatable by cutaneous liquid, so that the controlled access of skin moisture into the matrix is effected, and the islands thus absorb moisture so that a system-controlled intended super-saturation with active substance takes place, resulting in increased pharmaceutical release.

It can therefore be seen that according to these patentees, in order to be effective, the active material is incorporated into the base material of the islands, which is described as

> a variety of pharmaceutical auxiliaries which are swellable in water, such as, e.g., polyvinyl pyrrolidone, polyacrylic acid, polyvinyl alcohol,

> cellulose and its derivatives, naturally occurring slime formers, e.g., agar (agar), guar gum, and gum arabic, but as well inorganic materials, such as kaolin or bentonite are suitable components...

The polymer compositions of the present invention are entirely different. The overall thrust of the present invention is thus one which permits certain highly plasticizing drugs, such as selegiline, to be used with the adhesive systems thereof for direct application to the skin. This is only possible with the adhesives of the present invention, which are not swellable in water, as are the adhesives of Horstmann *et al*. Indeed, they are hydrophobic, as is now specifically required by claim 84. Thus, all of the specific polymers, such as those discussed at page 15, lines 11-24 of the present specification, and in particular the highly useful acrylic-based polymers hereof, are hydrophobic polymers and are quite unlike those used in the islands 14, 24 of Horstmann *et al*. Indeed, the teachings in Horstmann *et al*. with respect to using hydrophilic, or swellable polymers, would lead one directly away from the hydrophobic polymers of the present invention, and certainly do not obviate the present claims. While the Examiner has again referred to the disclosure beginning at page 15 of the specification, applicants have already pointed out that this disclosure, while broadly relating to certain aspects of the present invention, certainly does not refer or relate to the preferred embodiment of the present invention in which highly plasticized drugs such as selegiline and the like are employed. With that embodiment, the specification sets forth a specific disclosure beginning at page 18 with respect to the applicable adhesive compositions, specifying hydrophobic

substances such as the preferred acrylic-based polymers of claim 85. In these embodiments, so highly preferred by the applicants, in which applicants specify throughout this application that non-aqueous solvents are utilized, it is clear beyond question that one of ordinary skill in this art will readily recognize that it is only possible to prepare transdermal patches utilizing these highly plasticizing drugs if adhesive systems are employed, such as those disclosed herein, which are quite different from those pharmaceutical auxiliaries used in Horstmann *et al*. They cannot, for example, be swellable in water, but they must be hydrophobic in nature. Thus, all of the specific polymers, such as those discussed at page 15, lines 11-24 of the present specification, and in particular the highly useful acrylic-based polymers hereof, are hydrophobic polymers quite unlike those used in the islands 14, 24 of Horstmann *et al*. Indeed, the teachings in Horstmann *et al*. with respect to using hydrophilic, or swellable polymers, would teach one directly away from utilizing any of the hydrophobic polymers of the present invention, and certainly would not obviate the present claims.

It is also noted that the system described in Horstmann *et al*. requires water to activate the drug system thereof. They therefore control access of cutaneous liquids such as water by use of the system therein, including layer 13 for moisture access control. Moisture itself thus improves the activity of the drugs employed by Horstmann *et al*., and is considered critical to their cutaneous application.

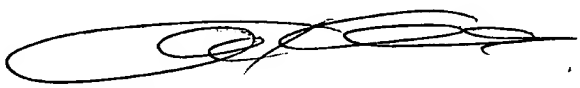
In the present application, on the other hand, only a single layer is necessary, and the matrix-forming agent, including the drugs, provides for adhesion to the skin itself.

It is therefore respectfully submitted that the claims now contained in this application clearly possess the requisite novelty, utility and unobviousness to warrant their immediate allowance, and such action is therefore respectfully solicited. Applicants reiterate their position that the finality of the rejection of July 12, 2000, is premature, but in any event request that the Examiner consider the present response as it is believed to overcome the objections which have been raised to the immediate allowance of this application. It is thus again requested that these rejections be withdrawn, and that this application be passed to issue. However, should the Examiner still not believe that such action can be taken at this time, it is respectfully requested that he telephone applicant's attorney at (908) 654-5000 in order to overcome any further objections which he might have to the allowance of these claims.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Respectfully submitted,

LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK, LLP



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